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A Longitudinal Study of the Kidney Function of the Chimpanzee (*Pan troglodytes*) in Comparison with Humans

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Summary: A prospective study of the kidney function of chimpanzees (*Pan troglodytes*) kept at the Hans Popper Primate Centre has been performed within the last 10 years. The aim of the study was to analyse urine samples for specific gravity, to determine serum creatinine, serum urea, and urinary creatinine, and to calculate creatinine clearance and reference values for healthy chimpanzees. From 1750 urine specimens of adolescent and 568 of infant chimpanzees a mean specific gravity value of 1.013 ± 0.006 (standard deviation) kg/l and 1.007 ± 0.003 (standard deviation) kg/l, respectively, was calculated. Serum creatinine was determined in 1864 single samples from 52 chimpanzees; a median value of 101.8 µmol/l (P (5%) 79.6 µmol/l, P (95%) 139.7 µmol/l) was calculated, which is higher than that in humans. Serum urea tests (n = 1831) in the same 52 chimpanzees resulted in a median value of 2.01 mmol/l (P (5%) 0.86 mmol/l, P (95%) 4.78 mmol/l). The calculated median creatinine clearance value of 23.9 ml/min (P (5%) 4.4 ml/min, P (95%) 65.3 ml/min) is lower in chimpanzees than in man. A correction of the creatinine clearance values to the body surface area of 1.73 m^2, as routinely performed in humans, gave unusually high results, as there was no proper equation to calculate the surface area of chimpanzees. The use of estimation equations for creatinine clearance values of chimpanzees as developed for humans is therefore not recommended.

Introduction

Many studies of the kidney function of humans of all age groups have been published and are fundamental for the treatment of renal diseases and kidney transplantation (1, 2). Better understanding of the kidney function of chimpanzees may help in certain clinical conditions to treat these animals. The aim of this prospective study was to analyse the kidney function of chimpanzees, i. e. to measure the specific gravity of urine samples, to determine serum creatinine, serum urea and urinary creatinine, to calculate clearance values during a 10 year follow up period and to compare the results with data from healthy humans.

Materials and Methods

Chimpanzee facility

The study was performed within the last 10 years at the Hans Popper Primate Centre, Austria. All chimpanzees were kept at an animal biosafety level 3 and 4 (3) and registered at the International Species Information System (1201 Johnny Cake Ridge Road, Apple Valley, MN USA 55124-8151). The majority of the chimpanzees participated in safety and efficacy studies with candidate vaccines against hepatitis B and C and HIV-1 (4–6). All kidney function tests were performed during the study prephase or for diagnostic and therapeutic purposes. Blood sampling was performed under ketamine^T anaesthesia (10 mg/kg body weight i. m.) after a minimum fasting period of 12 hours. All animals were fed individually with fruits and vegetables, milk and milk products. No standard pellet food was supplied. Exercise was neither encouraged nor prohibited. There was no restriction of the availability of drinking of water, "infant tea" or fruit juices. Animals were not isolated in metabolic cages, and permanent urethral catheterization was not performed.

Urine sample collection and determination of the specific gravity

Urine specimens were collected routinely in three periods (7 a. m. to noon, noon to 5 p. m., 5 p. m. to 7 a. m. next day) or over 24 hours by special urine collection containers. No preservative was used. Loss of urine by evaporation during the collection period may be ignored because of the 80% humidity (simulation of a tropical climate) in the animal rooms (7). A loss of urine of up to 50% due to urination through the front cage panel was recorded by the animal keepers on 26 days. On these particular days the urine volume was always less than 500 ml. The median creatinine clearance value was calculated with and without the data from these 26 days. Neither concentration nor dilution studies were performed. All measurements were carried out using a Vogel urinometer in aliquots of 100 ml urine at a constant temperature of 28 °C at the end of the collection period. Since the urinometers used were calibrated at 20 °C, all measurements were corrected by 0.003 to compensate for the temperature difference (8).

Serum and urinary creatinine

Creatinine in the serum of chimpanzees was tested by the *Jaffe* method modified according to *Bartels* et al. (kinetic test; alkaline creatinine picrate complex without deproteinization) using a commercially available reagent kit (Boehringer Mannheim, Germany) with a reference range for men of 53–97 µmol/l and 44–80 µmol/l for women (9, 10, 11). All determinations were performed using a Beckman DU 70 spectrophotometer. Each morning after measuring the exact urine volume, urinary creatinine was tested in a 1 : 50 dilution of one aliquot of the collected urine, using the same method as for the determination of serum creatinine. The reference range for the 24-hour urinary creatinine of humans was given by the manufacturer as 8.84–13.3 mmol.

Serum urea

For determination of serum urea a commercially available reagent kit from Boehringer Mannheim (enzymatic colorimetric method) was used. In this indirect method hydrolysis of urea is catalysed by urease. The reaction of the formed ammonium ions with salicylate and hypochlorite generates a green dye. As defined by the manufacturer the reference range for human serum was 1.7–8.3 mmol/l (12).

Calculation of the creatinine clearance

The clearance values were calculated using the formula.

$$\text{ml/min} = \frac{\text{urine volume per minute} \times \text{urine creatinine}}{\text{serum creatinine}}$$

In humans the value is routinely corrected to a body surface area of 1.73 m^2. Based on a body surface area of 1.73 m^2 the creatinine clearance reference range given by the manufacturer was 98–156 ml/min for men and 95–160 ml/min for women (13). Lower reference ranges like 85–124 ml/min for men and 75–115 ml/min for women were reported by other authors (1, 14).

Serum alanine aminotransferase (EC 2.6.1.2)

Alanine aminotransferase was determined using commercially available reagent kits (Boehringer Mannheim; optimized method of the German Society of Clinical Chemistry) at a reaction temperature of 25 °C (15). The reference serum alanine aminotransferase range of healthy chimpanzees was 4–20 U/l (16).

Serum γ-glutamyltransferase (EC 2.3.2.2)

γ-Glutamyltransferase was determined using commercially available reagent kits (Boehringer Mannheim) with a reaction temperature of 25 °C (17). The normal range of serum γ-glutamyltransferase in healthy chimpanzees was 4–20 U/l (18).

Quality control programmes

Precinorm® and Precipath® (Boehringer Mannheim, Germany) were used as internal quality control sera for spectrophotometric tests. Test results of a test series were considered as valid, if the results of both internal control sera were within the target values defined by the manufacturer and the intra-assay coefficient of variation was less than 5%. Invalid series were repeated on the same day. The imprecision of the determination of alanine aminotransferase showed an intra-assay coefficient of variation of less than 5% and an inter-assay coefficient of variation of 4% to 6% for the range 5 U/l to 100 U/l. Similar values were obtained for the determination of γ-glutamyltransferase. The imprecision of the creatinine and urea determination showed an intra- and inter-assay coefficient of variation of 5% to 8%. External quality control was performed by participation in a proficiency test programme organized since 1982 by the Austrian Society for Quality Assurance and Standardization of Analysis in the Clinical Laboratory. This control programme included routine measurement of alanine aminotransferase, γ-glutamyltransferase and creatinine in two unknown serum specimens six times per year. All data were evaluated by the Austrian Society for Quality Assurance and Standardization of Analysis in the Clinical Laboratory. Through the entire study, all test results of the codified quality control samples were within the range of the mean value plus/minus two standard deviations calculated from the data of all laboratories using the same method.

Statistical evaluations

All data were statistically evaluated using commercially available computer programs such as Lotus 1-2-3®, PFS Professional file® and GB-STAT®. Results were tested for normal distribution (19). *Spearman* rank correlation method was used for calculation of correlation (20). The sign test according to *Dixon & Mood* (21) and U-test according to *Wilcoxon, Mann* and *Whitney* (22) were used as non-parametric tests for comparison of two groups. Reference ranges were expressed as mean ± standard deviation when a normal distribution of the data was observed. Otherwise the median, the 5th (P 5%) and 95th (P 95%) percentile were calculated.

Results

Animal characteristics and results are summarized in table 1.

Specific gravity

A total of 1750 samples of 8 adolescent and 568 samples of 4 chimpanzees 2 to 4 years old were evaluated. The mean value of the specific gravity calculated per animal was in the range 1.006 to 1.017 kg/l with a standard deviation in the range 0.003 to 0.007 kg/l. The mean value calculated for all 8 adolescent animals was 1.013 ± 0.006 (standard deviation) kg/l with a maximum single value of 1.033 kg/l. Younger animals showed significantly lower levels. Five hundred and sixty-eight tests of 2 to 4 year-old animals resulted in a mean value of 1.007 ± 0.003 (standard deviation) kg/l with a maximum of 1.027 kg/l.

Serum creatinine concentrations

A total of 1864 serum samples from 52 chimpanzees were tested. The distribution of data was nearly normal (see fig. 1). The median creatinine value of all animals, independent of their body weight, was 101.8 µmol/l (P (5%) 79.6 µmol/l, P (95%) 139.7 µmol/l) with a minimum value of 36.2 µmol/l and a maximum value of 208.6 µmol/l. After stratification of all serum creatinine data into 6 classes according to the body weight of the chimpanzees at the time the blood sample was taken

Tab. 1 Creatinine clearance data of chimpanzees.
Calculated median and 5th to 95th percentile range of creatinine clearance of 158 samples of 9 chimpanzees.

	Median	Percentiles	
		5th	95th
Serum creatinine (µmol/l)	95.0	64.5	132.6
Volume of urine (ml/24 h)	850	300	1700
Urinary creatinine (mmol/l)	3.79	0.66	11.6
Urinary creatinine (mmol/24 h)	2.94	0.60	5.95
Creatinine clearance (ml/min)	22.5	4.0	62.5
Body weight (kg)	29.6	15.0	38.0
Height (cm)[a]	54.3	38.6	119
Body surface area (m^2)[b]	0.56	0.40	0.94
Age (years)	2	1	9

[a] Height of the chimpanzees from head to heel.
[b] body surface area in m^2 of the chimpanzees using the formula according to *Du Bois* (23).

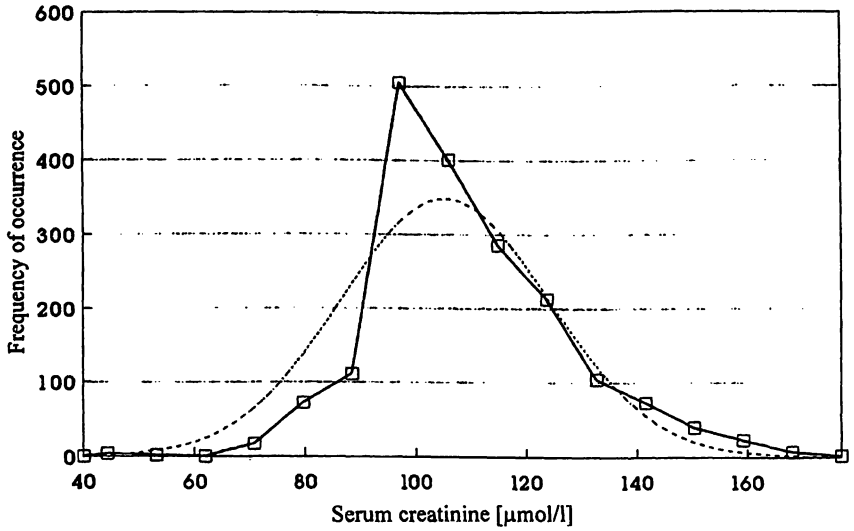

Fig. 1 Frequency distribution of serum creatinine values of chimpanzees.
Distribution of 1864 serum creatinine values (µmol/l) of 52 chimpanzees in comparison with the expected normal distribution.
----- = expected normal distribution
—— = actual serum creatinine distribution.

(class width 10 kg), a relation between the median value of serum creatinine of the class and the body weight was observed. The group with the lowest body weight (less than 10 kg) had a serum creatinine median value of 78.7 µmol/l (P (5%) 69.8 µmol/l, P (95%) 96.4 µmol/l), the group with a body weight between 51 and 60 kg a median value of 124.6 µmol/l (P (5%) 98.1 µmol/l, P (95%) 153.8 µmol/l). Using the *Spearman* rank correlation test, a positive correlation ($R_s = 0.5897$, $p < 0.0001$) between serum creatinine data and the body weight of all chimpanzees could be confirmed. In addition to the median value, results are shown in table 2 as mean value plus/minus standard deviation for purposes of comparison with reference literature.

Serum urea levels

Data from 1831 samples from 52 animals showed a nearly normal distribution (see fig. 2). The calculated median value was 2.01 mmol/l (P (5%) 0.86 mmol/l, P (95%) 4.78 mmol/l). In contrast to serum creatinine there was a negative correlation (*Spearman* rank test) between serum urea concentration and body weight ($R_s = -0.2293$, $p < 0.0001$).

Urinary creatinine

The urinary creatinine of 2278 urine samples from 52 animals showed a median value of 4.29 mmol/l with a P (5%) of 1.07 mmol/l and a P (95%) of 11.48 mmol/l. The median 24-hour creatinine value was 4.03 mmol (P (5%) 0.7 mmol, P (95%) 9.9 mmol).

Creatinine clearance

Creatinine clearance was calculated on 158 samples from 9 chimpanzees. The median urine volume was 850 ml (P (5%) 300 ml, P (95%) 1700 ml), the median urinary creatinine concentration was 3.79 mmol/l (P (5%) 0.66 mmol/l, P (95%) 11.6 mmol/l, the median 24-hour urinary creatinine excretion was 2.94 mmol (P (5%) 0.6 mmol, P (95%) 5.95 mmol), and the median clearance value was 22.5 ml/min (P (5%) 4.0 ml/min, P (95%) 62.5 ml/min). In 26 cases the volume of the urine samples was less than 500 ml in 24 hours as recorded by the animal keepers. Those cases were excluded from further evaluation. The recalculated clearance value resulted in a median value of 24.2 ml/min (P (5%) 5.11 ml/min, P (95%) 69.9 ml/min and a minimum of 3.0 ml/min and a

Tab. 2 Comparison of reference values calculated for chimpanzees and humans.
Chimpanzee reference values were calculated from the data of the 10 year study and compared with published data for humans (11, 12, 13).

	Chimpanzees				Humans	
	Median	P 5%	P 95%	Mean ± SD	Reference range	
Serum creatinine (µmol/l)	101.8	79.6	139.7	86.7 −123.9	53 − 97	male
					44 − 80	female
Serum urea (mmol/l)	2.01	0.86	4.78	1.05− 3.65	1.7 − 8.3	
Urinary creatinine (mmol/24 h)	4.03	0.7	9.9	0.51− 9.79	8.84− 13.3	
Creatinine clearance (ml/min)	22.5	4.0	62.5	8.3 − 49.5	98 −156[a]	male
					95 −160[a]	female

[a] corrected to body surface area of 1.73 m^2.

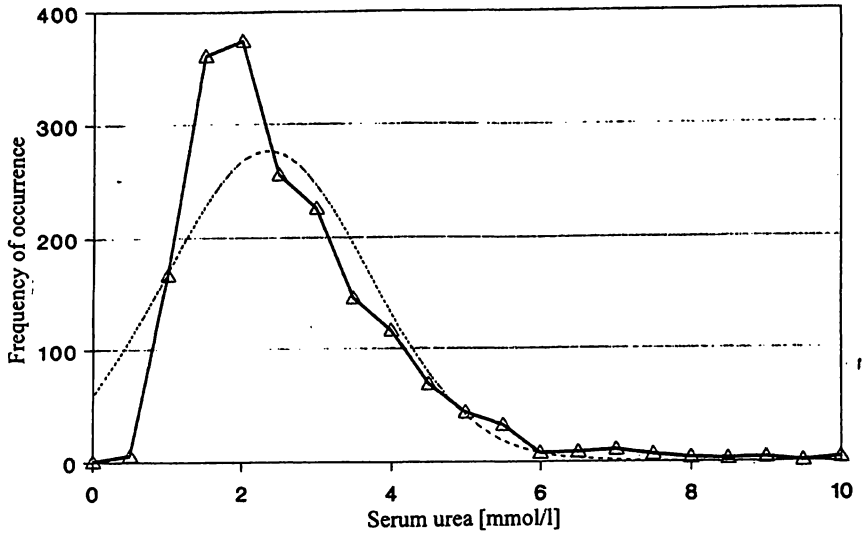

Fig. 2 Frequency distribution of serum urea values of chimpanzees.
Distribution of 1831 serum urea values (mmol/l) of 52 chimpanzees in comparison with the expected normal distribution.
----- = expected normal distribution
—— = actual serum creatinine distribution.

maximum of 122 ml/min. A significant difference between the median value of the creatinine clearance calculated from 158 cases and the median value calculated after exclusion of 26 cases with urine volume less than 500 ml in 24 hours could not be demonstrated. *Spearman* rank test showed a significant correlation between body weight and serum creatinine data ($R_s = 0.3943$, $p < 0.0001$), a correlation of $R_s = 0.2316$ (p 0.0034) between body weight and urinary creatinine values, but no correlation between body weight and creatinine clearance values ($R_s = 0.091$, p 0.2556). Creatinine clearance data correlated with the urinary creatinine values ($R_s = 0.7338$, $p < 0.0001$), and with the urine volume ($R_s = 0.3571$, $p < 0.0001$), but there was no correlation with serum creatinine concentrations, age, height and estimated surface area of chimpanzees.

To check the influence of the muscle mass on the creatinine clearance values, an attempt was made to correct the results to the height of the chimpanzee (head to heel height), the body weight and the body surface. This calculation included 132 test data. At the time of the clearance tests the median height of the animals was 54.3 cm (P (5%) 38.6 cm, P (95%) 119.2 cm). The median creatinine clearance value per cm was 0.39 ml/min. By correcting the data to the average human height of 170 cm, a median of 66.3 ml/min was calculated. The median clearance per kg body weight was 0.99 ml/min. Correction to 70 kg, the average body weight of humans with a height of 170 cm, resulted in a median of 69.4 ml/min.

Calculation of the body surface area of the chimpanzees using the formula of *Du Bois* (23) gave a median value of the surface area of 0.56 m^2 with a minimum of 0.10 m^2 and a maximum of 1.14 m^2. Correction of all data to a body surface area of 1.73 m^2 as used in humans resulted in a median of 70.9 ml/min.

Discussion

In the past 25 years, chimpanzees have frequently been used in preclinical trials to determine the safety and efficacy of plasma derivatives and hepatitis vaccines (24). Since 1983 more than 120 chimpanzees have been inoculated with HIV-1 (25). One might expect reference values of the renal function of chimpanzees to be available by now. Yet, there are hardly any publications comparing the kidney function of chimpanzees with humans. In three studies carried out between 1944 and 1964 the urinary specific gravity was investigated. *Hamlin* and coworkers (26) reported a mean value for the urinary specific gravity of 1.025 (standard deviation 0.006) kg/l with a range of 1.014 to 1.032 kg/l from a study of 9 chimpanzees. In a concentration trial performed by *Archibald* and coworkers in 1961, an increase from 1.013 to 1.031 kg/l was observed (27). A similar increase of the urinary specific gravity was reported 17 years earlier after 84 hours of dehydration of 12 chimpanzees (28).

The calculated reference range (mean ± standard deviation) of the urinary specific gravity data of adolescent chimpanzees in this study was lower than the values published for chimpanzees as described above. One reason for the difference might be the small number of test samples in the published studies, another one that the results were not stratified into age groups. The range for adult humans with normal fluid intake is between 1.003 and 1.029 kg/l. With increasing age in humans a range of 1.016 to 1.022 kg/l is seen. In the chimpanzees of this study, a dependency of specific gravity on age was observed. Animals two to four years old showed a lower specific gravity than the older ones.

The median value of the creatinine concentration of the tested chimpanzees was higher (median 101.8 µmol/l, P (5%) 79.6 µmol/l, P (95%) 139.7 µmol/l) than that of humans. The extent of the difference depended on the

reference range taken for comparison. The creatinine values of chimpanzees were higher, if compared with the reference range given by the manufacturer of the reagent kit at the beginning of the study (11). Recently the range was changed to an upper normal limit of 115 µmol/l for men < 50 years and to 97 µmol for women (29). However, the range of the serum creatinine concentration of chimpanzees was still higher than that of humans. It was necessary to investigate whether the higher values observed in chimpanzees were caused by non-creatinine substances. It is known that an unspecific elevation of reported serum creatinine values in human subjects may be caused by non-creatinine substances such as uric acid, glucose and numerous cephalosporin antibiotics, and may occur in cases of ketonuria, lipaemia and haemolysis (30–33). All these causes of unspecific elevated serum creatinine concentrations in chimpanzees could be excluded. Finally a comparison of the *Jaffe* method and an enzymatic test method was carried out to examine whether the higher values were caused by the *Jaffe* method itself. A limited number of serum and urine samples of chimpanzees randomly chosen was tested for creatinine concentration by simultaneously applying an enzymatic test (Creatinine PAP® reagent kit from Boehringer Mannheim; creatininase, *p*-aminophenazone) and the *Jaffe* method used in this study (34). A positive correlation of the creatinine values of both methods ($R_s = 0.87$, $p < 0.0001$) was observed. There was no significant difference between the two assays.

Because some of the animals were involved in transmission studies with hepatitis B and hepatitis C virus, the influence of an acute or chronic hepatitis B and C on the serum creatinine concentration was investigated. In humans, a low creatinine result may be caused by hepatic failure due to fulminant hepatitis or advanced biliary cirrhosis, because of decreased hepatic production of creatine or reduced muscle mass (35). Although histological findings of the liver biopsies taken regularly during hepatitis studies excluded such severe liver diseases, the median value after exclusion of data sets with elevated alanine aminotransferase and γ-glutamyltransferase in the serum of the chimpanzees (> 20 U/l) was recalculated. However, this procedure did not significantly change the median values per body weight group or the median value of serum creatinine of all tested chimpanzees. After deletion of 303 data sets with elevated alanine aminotransferase results and deletion of 524 data sets of elevated γ-glutamyltransferase, the median value decreased insignificantly from 101.8 µmol/l to 101.7 µmol/l and finally to 99.0 µmol/l creatinine.

In the last 30 years six studies only, five of them published before 1975, have reported values for the serum creatinine concentration of chimpanzees. In half of the investigations a Technicon Autoanalyzer® system was used and mean values in the range 61.9 µmol/l to 79.6 µmol/l (standard deviation 26.5 µmol/l) were obtained (36, 37, 38). In two studies performed in 1967 higher mean values of the serum creatinine concentration of chimpanzees were reported. *Hodson* et al. (39) gave a reference range of 106 µmol/l to 114.9 µmol/l when twelve chimpanzees with an age of three to six years were tested. *Burns* (40) reported a creatinine mean value of 126.4 µmol/l for juvenile (n = 7) and 111.4 µmol/l with a range of 95.5 µmol/l to 117.6 µmol/l for mature chimpanzees (n = 27) with a body weight of 8 kg to 63 kg. *Hainsey* and coworkers (41) reported in 1993 a reference range of 35.4–106 µmol/l when 26 chimpanzees were tested by a kinetic *Jaffe* method with a fully automated benchtop analyser (Hoffmann-La Roche). For the male chimpanzees of this group (n = 8) a higher range of serum creatinine (mean ± 2 standard deviations: 44.2 µmol/l–114.9 µmol/l) was calculated than for the 18 females. Since no indication of the body weight can be found in the report by *Hainsey* and coworkers, it is questionable whether a correlation between body weight and serum creatinine concentration was established. It might be speculated that the reason for the lower range is that a larger group of animals was used with a body weight less than 20 kg. Another reason for the discrepancy, as compared with the present study, might lie in the different diet of the chimpanzees. The chimpanzees tested in the *Hainsey* study were mainly fed with a commercial monkey chow (Purina Mills, USA) and the diet was only occasionally supplemented with fruits and vegetables. This is significantly different from the nutrition of the chimpanzees of the Hans Popper Primate Centre, where nutrition mainly consists of fruits and vegetables. The difference in the serum creatinine range between the two studies might also be due to the different reaction temperatures of the test method (25 °C Boehringer Mannheim vs. 37 °C Hoffmann-La Roche). For purposes of comparison the mean value plus/minus standard deviation is stated in addition to the median, 5th percentile and 95th percentile value in table 2. The higher mean value of the serum creatinine concentration obtained in this study compared with humans was in agreement with the mean values described by *Hodson* et al. (39) and *Burns* et al. (40). The differences in the serum creatinine values between chimpanzees and human subjects might be explained by the larger muscle mass of the chimpanzees. A positive correlation was demonstrated between serum creatinine and body weight of chimpanzees ($R_s = 0.5897$, $p < 0.0001$). This finding was supported by the report from *DiGiacomo* and coworkers (37) who determined the serum creatinine concentration of 74 chimpanzees aged two to eight years and observed a positive correlation ($R = 0.50$, $p < 0.005$) between creatinine values and body weight.

In both humans and chimpanzees, as soon as a stable body weight is attained and the process of growth is completed, there is only a minimal fluctuation in the

individual creatinine concentration (42). In male chimpanzees, the process of growth is completed at the age of 10 to 12 years. According to unpublished investigations at the Hans Popper Primate Centre (2058 measurements of body weight and height) the growth of female chimpanzees finishes one to two years earlier, i. e. approximately at the age of 8 to 9. Thus, renal function values are stabilized between the 8th and 12th year.

The urea concentration of the tested serum samples was significantly lower than in humans due to the low protein intake. The influence of hepatitis transmission studies on the serum urea median value was investigated by deletion of 299 data sets with an elevated alanine aminotransferase value (> 20 U/l) and 523 data sets with elevated γ-glutamyltransferase and recalculation of the median value. There was no change of the value obtained before and after this procedure (2.01 mmol/l).

Individual elevated urea values up to 12.8 mmol/l were occasionally observed due to a protein-rich diet which was part of a "creative feeding programme" at the Hans Popper Primate Centre.

The amount of urinary creatinine excreted in 24 hours by chimpanzees (median 4.03 mmol, P (5%) 0.7 mmol, P (95%) 9.9 mmol) was significantly lower than that of healthy human subjects (8.84−13.3 mmol).

All creatinine clearance results in humans were corrected to the body surface area of 1.73 m^2 according to the formula of *Du Bois* (23) or similar nomograms. The creatinine clearance in chimpanzees, if not corrected to the body surface area of 1.73 m^2, was significantly lower than in humans. An attempt was made to correct the clearance values to the body size (weight and height) and to the body surface area. The lowest clearance values were obtained by correction to 70 kg body weight, the highest by correcting to the surface area of 1.73 m^2. All 3 corrections showed maximum results of 236, 340 and 358 ml/min and would be about 3 times above the human upper limit. It is evident that the formula of *Du Bois* (23) cannot be used. The original paper describes a nomogram together with the formula giving a limit to the height of 100 to 200 cm and to the body weight of 20 to 110 kg. *Du Bois* recommends that the simple formula should not be used for people with unusual body shape, because wrong results may be obtained. Despite the biochemical similarities between humans and chimpanzees, the body shape distinctly differs in terms of the length of the trunk, the arms and the circumference of the upper arms.

Discrepant results were also obtained using other estimation equations to calculate the creatinine clearance. *O'Connell* (43) reported in 1993 that no significant differences existed between estimated and measured clearance values in humans when total body weight was used with the *Jelliffe* formula (44) and the *Cockroft-Gault* equation (45), and when "dosing weight" was used with *Hull* (46) and *Mawer* (47) equations. Creatinine clearance of chimpanzees was calculated with the aid of all 4 equations, and the results were significantly different from the measured values. Therefore the published estimation formulae cannot be used for chimpanzees.

In 1957, *Gagnon* (48) published creatinine clearance mean values of 6 chimpanzees of 2.36 ml/min × kg, with plasma creatinine results within a range 53 to 88 µmol/l. However, in 1964 *Scott* (49) measured, in 20 immature chimpanzees with permanent urethral catheterization, a creatinine clearance of 2.41 ml/min × kg in males and 1.52 ml/min × kg in females for the first 6 hour period. The values decreased to 2.02 and 1.45 ml/min × kg during the last 6 hours of a 24 hour collection period. Although the animals were restrained in a sitting position for 24 hours, the creatinine clearance results published 30 years ago produced similar results to those obtained recently in a longitudinal study covering a period of 10 years (median of serum creatinine 0.99 ml/min × kg, P (5%) 0.15 ml/min × kg, P (95%) 2.14 ml/min × kg). The difference in the results obtained might be attributable to the age of the animals and the use of a different method to determine the creatinine concentration.

The implication of the lower clearance values of chimpanzees is not known yet. It may have an important impact on the dosage of certain antibiotics or other drugs when a dosage recommended for humans is administered. The different renal function may inadvertently prolong the serum concentration of the administered antibiotic.

In general, the measurement of serum and urinary creatinine of chimpanzees resulted in values similar to humans, yet there are small but important differences. Specific gravity of the 24 hour urine seems to be lower than that of humans. Serum creatinine corresponds to the body weight and is significantly higher, while urinary creatinine is lower than in man. Because a correction of the clearance to the body surface area of chimpanzees using the formula of *Du Bois* is impossible, a direct comparison of corrected values with humans is not relevant. The use of estimation equations results in widely distributed values which do not correlate with the measured values. Measurement of urea is not a reliable tool for checking renal function in chimpanzees, due to their low protein diet.

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